Effects of COVID-19 and pneumococcal conjugate vaccines on hospitalized older COVID-19 patients in Türkiye

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Abstract

Background: The COVID-19 vaccine, CoronaVac, and pneumococcal conjugate vaccine, PCV13, are part of Türkiye's adult immunization programme to reduce COVID-19 severity and mortality among older adults.

Aim: To evaluate the effects of CoronaVac and PCV13 vaccines on hospitalized patients aged ≥ 65 years in Türkiye.

Methods: This retrospective descriptive study included 365 patients aged ≥ 65 years admitted to the COVID-19 wards and intensive care unit of Şişli Hamidiye Etfal Training and Research Hospital in Türkiye between March and June 2021. We evaluated vaccine efficacy among patients at ≥ 14 days and < 14 days after the second dose. We analysed the data using SPSS version 20.0 and compared proportions in independent groups using χ^2 test. $P < 0.05$ was considered statistically significant.

Results: Intensive care unit admission was lower (25.3%) among patients vaccinated with CoronaVac than among unvaccinated patients (38.5%), and mortality rate was significantly lower (16.9% vs 32.7%) among vaccinated patients. Mortality decreased significantly with the number of vaccine doses. No significant relationship was found between PCV13 vaccination and mortality or intensive care unit admission, but mortality was lower among vaccinated patients.

Conclusion: CoronaVac significantly reduced intensive care unit admissions and mortality among older COVID-19 patients. Although PCV13 did not show a significant reduction in mortality, its observed benefit supports continued pneumococcal vaccination among older populations.

Keywords: COVID-19, vaccination, vaccine, CoronaVac, PCV13, geriatric, mortality, Türkiye

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Introduction

According to WHO, lower respiratory tract infections are the fourth most common cause of mortality, and the third most common according to the Turkish Statistical Institute (*1*, *2*). The severity of viral and bacterial infections increases markedly in older adults compared with younger individuals, often resulting in more acute and prolonged sequelae (*3*–*5*).

Age-related decline and dysregulation of immune function have serious consequences for COVID-19 in older adults and play an important role in increased vulnerability to COVID-19 (*6*). CoronaVac (inactivated SARS-CoV-2 vaccine; ISV) was the first vaccine to arrive in Türkiye for immunization against COVID-19 and was initially administered to patients aged ≥ 65 years. It has been shown that this vaccine reduces symptoms and hospitalization, especially in people aged > 70 years (*7*), as well as mortality in hospitalized patients (*8*).

One factor influencing the length of hospital stay is secondary bacterial infections, which are commonly observed following COVID-19 (*9*, *10*), including community-acquired pneumonia caused by *Streptococcus pneumoniae*. Pneumococcal vaccination is part of the adult immunization programme in Türkiye, and the pneumococcal conjugate vaccine (PCV13) was recommended during the COVID-19 pandemic (*11*). The purpose of this study was to assess how PCV13 and CoronaVac affected the progression of COVID-19 infection in individuals aged ≥ 65 years who were admitted to hospital.

Methods

Patient selection and study design

This was a retrospective, descriptive single centre study. A total of 399 patients aged ≥ 65 years were admitted to the COVID-19 inpatient wards and intensive care unit (ICU) of Şişli Hamidiye Etfal Training and Research Hospital between March 1 and June 1 2021. Eight patients who had received an mRNA vaccine were excluded from the study, along with 26 patients who were moved to ICUs in other hospitals and could not be followed up. Therefore, data from 365 patients were used in the study. The study was approved by the Health Sciences University Şişli Hamidiye Etfal Health Practice and Research Center Ethics Committee (dated 8 June 2021, numbered 3323).

Data collection tools

We recorded patients' age, gender, COVID-19 polymerase chain reaction (PCR) positivity, number of days in the COVID-19 ward, number of days in ICU, timing of COVID-19 vaccination, pneumococcal vaccination status, and overall length of hospital stay.

CoronaVac was the first COVID-19 vaccine to be given in Türkiye. Priority was given to people who requested vaccination and those aged ≥ 65 years. In Türkiye, adult immunization has been increasing steadily. PCV13 and polysaccharide pneumococcal vaccine (PPSV23) are recommended for immunization against pneumococcal infections. PCV13 has been offered free since 2016 to all individuals aged ≥ 65 years, as well as to those aged 18–65 years with risk factors such as diabetes or chronic kidney disease. PCV13 is registered through the immunization tracking system and administered in immunization clinics. PPSV23 is not yet provided free and the vaccination tracking system data are incomplete (*12*, *13*).

We retrospectively investigated the CoronaVac and PCV13 vaccination status of the patients. Vaccine efficacy evaluated 14 days after the second dose of CoronaVac was 83.5% in a previous study (*14*). After deciding that 14 days was the minimal amount of time needed for the COVID-19 vaccine to take effect, we divided the patients who received 2 doses of CoronaVac into 2 groups: those at ≥ 14 days after the second dose and those at < 14 days after the second dose.

Statistical analysis

SPSS 20.0 was used for statistical analysis. Numbers and percentages were given for categorical variables, and mean and standard deviation, and minimum and maximum values for numerical variables. Comparisons between 2 independent groups were made when numerical variables met a normal distribution, and with the Mann-Whitney U test when they did not meet a normal distribution. Proportions in independent groups were compared using χ^2 test. $P < 0.05$ was considered statistically significant.

Results

The mean age of the 365 patients was 75.94 ± 8.184 (65–104) years. There were 186 (51.0%) women and 179 (49.0%) men. One hundred and six patients (29.0%) were referred to ICU. The mean period of hospitalization in the COVID-19 ward was 9.58 ± 6.634 (1–37) days. The average length of stay in the ICU was 9.10 ± 6.926 (0–67) days. The mean total hospital stay was 12.6795 ± 8.56993 (1–68) days. Before hospitalization, 104 (28.5%) patients had never been vaccinated against COVID-19; 98 (26.8%) had received 1 dose and 154 (42.2%) received 2 doses of CoronaVac. There were 252 (69.0%) patients who had received at least 1 dose of CoronaVac before hospitalization. Two hundred and forty-three (66.6%) patients were hospitalized before 14 days after COVID-19 vaccination. Two hundred and eighty-seven (78.6%) patients were PCR positive. There was a significant relationship between ICU referral and being PCR positive ($P = 0.007$), and 93 (87.7%) of those referred to ICU were PCR positive. Age did not significantly correlate with the number of days in the COVID-19 ward, the number of days in ICU, or the overall number of days in hospital ($P = 0.704$, 0.804 and 0.620, respectively).

The mortality rate after COVID-19 infection was 21.4% ($n = 78$). The relationship between age and mortality was significant ($P = 0.000$). The mean age of patients who died due to COVID-19 infection was 79.14 ± 9.062 (65–100) years. The mean age of patients who recovered from COVID-19 infection and were released was 75.07 ± 7.718 (65–104) years. Mortality among patients who received

Table 1 ICU admission and mortality in COVID-19 patients

	ICU admission		*P*	Mortality		*P*
	Yes No. (%)	No No. (%)		Yes No. (%)	No No. (%)	
Gender						
Female	52 (28)	134 (72)	0.672	37 (19.9)	149 (80.1)	0.483
Male	54 (30.2)	125 (69.8)		41 (22.9)	138 (77.1)	
CoronaVac doses						
None	41 (36.3)	72 (63.7)	0.095	34 (30.1)	79 (69.9)	0.021
1	28 (28.6)	70 (71.4)		19 (19.4)	79 (80.6)	
2	37 (24.0)	117 (76.0)		25 (16.2)	129 (83.8)	
Minimum time required for COVID-19 vaccine effectiveness						
Completed	30 (24.6)	92 (75.4)	0.184	55 (22.6)	188 (77.4)	0.406
Not completed	76 (31.3)	167 (68.7)		23 (18.9)	99 (81.1)	
PCR						
Positive	93 (32.4)	194 (67.6)	0.007	67 (23.3)	220 (76.7)	0.077
Negative	13 (16.7)	65 (83.3)		11 (14.1)	67 (85.9)	
PCV13						
Unvaccinated	75 (29.0)	184 (71.0)	0.956	60 (23.2)	199 (76.8)	0.191
Vaccinated	31 (29.2)	75 (70.8)		18 (17.0)	88 (83.0)	

ICU = intensive care unit; ISV = inactivated SARS-CoV-2 vaccine; PCR = polymerase chain reaction; PCV13 = pneumococcal conjugate vaccine.

at least 1 dose of CoronaVac was significantly lower than that of patients who did not receive CoronaVac (P = 0.001).

Among those who received CoronaVac 25.3% were admitted to the ICU, and 38.5% of unvaccinated individuals were admitted to the ICU. A significant relationship was found between receiving the COVID-19 vaccine and ICU admission (P = 0.012). Mortality rate was 16.9% (n = 44) among patients who received COVID-19 vaccine compared with 32.7% (n = 34) among those not vaccinated. There was a significant inverse relationship between being vaccinated against COVID-19 and mortality (P = 0.001). There was a significant decrease in mortality rate as the number of vaccine doses increased (P = 0.021). The risk of death was 2.035 times higher for those who were not vaccinated than for those who were vaccinated (P = 0.007), regardless of dosage. Compared with patients who received a single dose of vaccine, those who were not vaccinated had a 1.789-fold increased risk of dying (P = 0.74). Patients who were not vaccinated had a 2.212-fold increased chance of dying in comparison with those who received 2 doses of the vaccine (P = 0.007). There was no significant association between time after the second dose of CoronaVac and mortality or referral to ICU. Although mortality was higher among patients who had not received PCV13, the difference was not significant (P = 0.191).

Table 2 shows that there was a significant relationship between minimum time required for COVID-19 vaccine effectiveness and total hospital stay (P = 0.001). There was a significant correlation between having at least 1 dose of CoronaVac and the total number of days in hospital (P = 0.019). There was a significant relationship between PCR positivity and total number of days in hospital (P = 0.006). A significant relationship was found between COVID-19 ward stay, ICU stay, total hospital stay and COVID-19 mortality.

Discussion

We evaluated the effect of CoronaVac and PCV13 on the course of COVID-19 in hospitalized patients aged ≥ 65 years. Mortality was 2.212 times higher among unvaccinated patients than among those who received 2 doses of vaccine, and as the number of doses increased, mortality decreased.

In a previous study among individuals aged > 18 years, mortality was lower after 2 doses of CoronaVac than among unvaccinated individuals (*15*). Another study reported that the risk of mortality due to COVID-19 among unvaccinated individuals aged ≥ 60 years was 21.3 times higher than among those who had received 2 or 3 doses of the vaccine (*16*). Even with a single dose, the risk of mortality was 2.3 times lower than among unvaccinated people.

We found no significant relationship between time of effectiveness after vaccination and mortality and ICU admission, which contrasts with the study by Faria et al. (*17*). As a result of immunosenescence, older people typically have a lower immunological response to infection or immunization (*18*). The risk of serious disease and mortality due to COVID-19 is higher among people aged ≥ 60 years, especially those with comorbidities (*18*). The lack of a significant relationship in our findings may be because our patients were aged ≥ 65 years, potentially had comorbidities, and experienced an age-related decline in immune response.

We found a relationship between PCR positivity and ICU admission and mortality. A previous study showed no significant correlation between PCR positivity and high-resolution computed tomography severity score (*19*). However, PCR positivity can be an indicator of viral load and its association with high-resolution computed tomography severity score. Liu and colleagues reported that patients with severe COVID-19 tend to have a higher viral load and longer duration of viral shedding, suggesting that the load of SARS-CoV-2 could be a useful marker for assessing disease severity and prognosis

Table 2 Length of stay in COVID-19 ward and ICU, and total hospitalization for COVID-19 patients

		Length of stay in COVID-19 ward (n = 365)			Length of stay in ICU (n = 106)			Total length of hospitalization (n = 365)		
		Mean	SD	*P*	Mean	SD	*P*	Mean	SD	*P*
At least 1 dose of CoronaVac	Vaccinated	9.27	5.985	0.620	9,58	6.415	0.610	11.7460	7.3312	0.019
	Unvaccinated	10.26	7.879		12.41	12.298		14.7611	10.5773	
Minimum time required for COVID-19 vaccine effectiveness	Completed	8.57	5.471	0.118	8.47	7.084	0.076	10.6475	6.97448	0.001
	Not completed	10.09	7.103		11.55	9.815		13.6996	9.111	
PCR positive	Yes	9.62	6.608	0.736	11.05	9.401	0.130	13.202	8.666	0.006
	No	9.42	6.770		8.00	7.348		10.7564	7.966	
Mortality	Yes	4.68	4.780	0.000	12.12	9.713	0.005	15.0897	10.501	0.009
	No	10.91	6.445		8.21	7.747		12.0244	7.859	
PCV13	Vaccinated	9.25	5.849	0.926	10.45	6.260	0.474	12.301	7.4567	0.982
	Unvaccinated	9.71	6.936		10.77	10.205		12.834	8.994	

ICU = intensive care unit; SARS-CoV-2 vaccine; PCR = polymerase chain reaction; PCV13 = pneumococcal conjugate vaccine.

(*20*). Our findings support the association between PCR positivity, viral load and disease severity among older people (*21*).

Throughout the pandemic, the value of adult vaccination was emphasized in Türkiye and the rest of the world. The significance of continuing adult vaccinations has been mentioned in the literature (*22*).

Respiratory infections caused by SARS-CoV-2 have been associated with secondary bacterial and fungal infections (*10*). *S. pneumoniae* is one of the bacteria that cause community-acquired pneumonia in Türkiye (*23*). Therefore, our study examined the PCV status of inpatients aged > 65 years. Although there was no apparent connection between mortality and PCV13 vaccination, individuals who received the vaccine had reduced mortality. Patients who received PCV13 had shorter hospital stay. It has been reported that patients who received PCV13 had lower rates of COVID-19 mortality and morbidity (*24*). Lack of data on patients' comorbidity and the length of time before hospital admission could explain the lack of a significant link.

The interactions between several vaccines have been examined in previous research (*25*, *26*). PCV13 had no relationship with mortality or ICU admission in our study. The lower mortality rates among patients who received PCV13 indicates the importance of its administration, although the association was not significant.

Our study had some limitations. First, some ICU patients were transferred to other hospitals and were lost to follow-up; therefore, details of their treatment plans and outcomes could not be obtained. Second, data were available for PCV13 but not for PPSV23. This could make it more difficult to assess vaccine efficacy in preventing pneumococcal infections. No additional tests were conducted to assess secondary infections, resulting in insufficient information about their frequency or impact.

A major strength of the study was that it investigated progression of COVID-19 among individuals aged ≥ 65 years, providing valuable insights specific to this age group.

Conclusion

In this study, we assessed the effects of CoronaVac and PCV13 on the progression of COVID-19 infection among hospitalized patients aged ≥ 65 years. Our findings indicate that vaccination, particularly with multiple doses of CoronaVac, significantly reduced ICU admission and mortality. Although no significant relationship was found between PCV13 and ICU admission or mortality, the lower mortality among those who had received PCV13 highlights the importance of continuing adult pneumococcal vaccination, especially among older people. These results emphasize the role of vaccination in improving health outcomes among older people, particularly those at higher risk of severe disease resulting from age-related immune decline and comorbidities.

Future studies should focus on collecting comprehensive comorbidity data, investigating secondary infections, assessing the interaction between vaccines such as PCV13 and PPSV23, conducting long-term follow-up, and evaluating the durability of vaccine-induced immunity, to better understand the role of vaccination in mitigating severe outcomes among older people during pandemics.

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Effets des vaccins contre la COVID-19 et des vaccins pneumococciques conjugués sur les patients âgés hospitalisés pour la COVID-19 en Türkiye

Résumé

Contexte : Le vaccin anti-COVID-19 (CoronaVac) et le vaccin antipneumococcique conjugué (PCV13), font partie du programme de vaccination des adultes de Türkiye visant à réduire la sévérité de la COVID-19 et la mortalité associée chez les personnes âgées.

Objectif : Évaluer les effets des vaccins CoronaVac et PCV13 sur les patients hospitalisés âgés de 65 ans ou plus en Türkiye.

Méthodes : La présente étude descriptive rétrospective a inclus 365 patients âgés de 65 ans ou plus admis dans les services de soins et l'unité de soins intensifs, dédiés à la prise en charge de la COVID-19, de l'hôpital de formation et de recherche Şişli Hamidiye Etfal en Türkiye entre mars et juin 2021. Nous avons évalué l'efficacité des vaccins chez les patients ayant reçu leur deuxième dose depuis 14 jours ou plus et chez ceux l'ayant reçue depuis moins de 14 jours. Nous avons analysé les données à l'aide du logiciel SPSS version 20.0 et comparé les proportions dans des groupes indépendants à l'aide du test χ^2. Une valeur *p* inférieure à 0,05 était considérée comme statistiquement significative.

Résultats : Le taux d'admission en unité de soins intensifs (25,3 %) était plus faible chez les patients vaccinés avec le CoronaVac que chez les non-vaccinés (38,5 %), et le taux de mortalité était significativement plus bas (16,9 % contre 32,7 %) chez les patients vaccinés. La mortalité diminuait considérablement avec le nombre de doses de vaccin. Aucune relation significative n'a été observée entre la vaccination PCV13 et la mortalité ou l'admission en unité de soins intensifs, mais la mortalité était plus faible chez les patients vaccinés.

Conclusion : Le CoronaVac a permis de réduire de façon significative les admissions en soins intensifs et la mortalité chez les patients âgés atteints de la COVID-19. Bien que le PCV13 n'ait pas montré de réduction significative de la mortalité, son bénéfice observé étaye la poursuite de la vaccination pneumococcique dans les populations plus âgées.

آثار لقاحات كوفيد19- والمكورات الرئوية المتقارنة على مرضى كوفيد- 19 المسنِّين النزلاء في مستشفيات تركيا

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الخلاصة

الخلفية: يُعَد لقاح كوفيد-19 (كورونافاك) واللقاح المتقارن للمكورات الرئوية (PCV13) جزءًا من برنامج تمنيع البالغين في تركيا، للحد من وخامة كوفيد-19 والوفيات بين كبار السن.

الأهداف: هدفت هذه الدراسة الى تقييم آثار لقاحي كورونافاك وPCV13 في المرضى نزلاء المستشفيات الذين تبلغ أعمارهم 65 عامًا أو أكثر في تركيا.

طرق البحث: شملت هذه الدراسة الوصفية الاسترجاعية 365 مريضًا تبلغ أعمارهم 65 عامًا أو أكبر ممَّن حُجزوا في أجنحة كوفيد-19 ووحدة الرعاية المركزة بمستشفى شيشلي حميدية إتفال للتدريب والبحث في تركيا في الفترة بين مارس/ آذار ويونيو/ حزيران 2021. وقيَّمنا نجاعة اللقاح بين المرضى خلال 14 يومًا أو أكثر، ونجاعته خلال أقل من 14 يومًا بعد الجرعة الثانية. وقد حلَّلنا البيانات بالإصدار 20.0 من برمجية SPSS، وقارنَّا النِّسَب في مجموعات مستقلة باختبار χ^2. وقد عُدت قيمة الاحتمال < 0.05 ذات دلالة إحصائية.

النتائج: كان الإدخال إلى وحدة الرعاية المركزة أقل (25.3٪) بين الذين حصلوا على لقاح كورونافاك مقارنة بالذين لم يحصلوا عليه (38.5٪)، وكان معدل الوفيات أقل كثيرًا (16.9٪ مقابل 32.7٪) بين المرضى الذين حصلوا على التطعيم. وقد انخفضت نسبة الوفيات انخفاضًا كبيرًا بسبب عدد جرعات اللقاح. ولكن لم يُعثَر على أي علاقة ذات دلالة بين التطعيم بلقاح PCV13 وبين معدل الوفيات أو الإدخال إلى وحدة الرعاية المركزة، إلا أن معدل الوفيات كان أقل بين المرضى الذين حصلوا على التطعيم.

الاستنتاجات: أدى التطعيم بلقاح كورونافاك إلى انخفاض ملحوظ في معدَّل الإدخال إلى وحدة الرعاية المركزة والوفيات بين مرضى كوفيد-19 الأكبر سنًّا. وعلى الرغم من أن لقاح PCV13 لم يكن له أثر كبير في انخفاض معدَّل الوفيات، فإن فوائده الملحوظة تؤيد مواصلة التطعيم به لمكافحة المكورات الرئوية بين المسنِّين.

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